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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/311,996
Filing Date: May 14, 1999
Appellant(s): VAISBERG ET AL.

Julie L. Heinrich
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12 August 2005 and the amended appeal brief filed 29 September 2005 appealing from the Office action mailed 13 March 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Pauwels et al. "Determination of the Mechanism of Action of Anticancer Drugs by Means of the Computer-Assisted Microscope Image Analysis of Feulgen-Stained Nuclei" Journal of Pharmacological and Toxicological Methods, Vol. 37, (1997), pages 105-115

Paull et al. "Display and Analysis of Patterns of Differential Activity of Drugs Against Human Tumor Cell Lines: Development of Mean Graph and COMPARE Algorithm" Journal of the National Cancer Institute, Vol. 81 (1989), pages 1088-1092

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 49-57, 60, 61, and 63-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to:

1) a computer program that executes a method of cell image analysis that includes a step reciting "wherein some of said features from a first cell type are combined with features from a second cell type to yield one or more composite descriptors" in claims 49-55 and 66;

2) a computer program that executes a method of cell image analysis that includes a step reciting "wherein some of said features from a first type are combined with features from a second cell type to yield one or more composite features" in claims56, 57, 60, and 61; and

3) a computer program that executes a method of cell image analysis that includes a step reciting "wherein at least some of said descriptors combine features from cells of different cell types" in claims 63-65.

The specification does not describe composite descriptors or descriptors which comprise features of different cell types.

Claims 49-57, 60, 61, and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pauwels et al. (Journal of Pharmacological and Toxicological Methods, Vol. 37, pages 105-115 (1997), cited as reference AE in the Information Disclosure Statement filed 14 May 1999) in view of Paull et al. (newly cited in this Office action).

The claims are drawn to a computer program on media that executes a cell image analysis method comprising steps of receiving images of components of a plurality of cells of different types that have been manipulated, producing composite descriptors that include information from cells of different types, and use of principal component analysis to produce a fingerprint of the effect of the manipulation on the different cell types. In some embodiments the components of the cells are organelles or nucleic acids, the manipulation is application of a chemical compound such as a drug, the information collected is relevant to toxicity or metabolism. In some embodiments the program predicts properties of a compound based on its effect on cells.

Pauwels et al. shows in the abstract and throughout a method of analyzing the effect of a variety of antitumor drugs on tumor cell lines by analysis of digital images of treated cells. Three cell lines and thirty drugs were examined. On page 107, Pauwels et al. details the computer mediated image analysis of the cells. Pauwels et al. determines 15 of parameters of the cells and derive data for the cells including nuclear area, DNA content, and chromatin texture. Pauwels et al. shows in figures 3-6 the results of principal component analysis for the drugs for each cell line. In figure 6 Pauwels et al. show that the analysis shows that classes of drugs with common features and modes of action can be determined by formation of centroids in the analysis. Pauwels et al. concludes on pages 112-114 that their method can be used to assign drugs to

classes of drugs on the basis of the effects of the drugs on treated cells as determined by their image analysis method. Pauwels et al. does not show descriptors or fingerprints that comprise information of a plurality of cell lines.

Paull et al. shows a computer program called COMPARE that analyzes the effect of antitumor drugs on a panel of 60 different tumor cell lines. The information obtained from the cell lines was growth inhibition. Paull et al. show on page 1089 that their method produces fingerprints for each drug tested that show a structure-function relationship. Paull et al. calculates statistical measures of growth inhibition that considers the effect of a drug on all cell lines tested in pages 1089-1091, and the data are summarized in Table 2. Paull et al. conclude that drugs with similar modes of action cluster with similar values on page 1092.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to write a computer program to perform the method of Pauwels et al. because Pauwels et al. shows use of algorithms to analyze cell image data and Paull et al. shows a computer program that performs similar analysis of drug treated tumor cell lines. It would have been further obvious to modify the method of Pauwels et al. by construction of descriptors or fingerprints derived from the plurality of tumor cell lines tested by Pauwels et al. because Paull et al. shows that consideration of data from a plurality of tumor cell lines allows for drugs to be clustered by mode of action or structure while considering their effects on a wide range of tumor cell types.

Claims 63 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pauwels et al. in view of Paull et al. as applied to claims 49-57, 60, 61, and 63-65 above, and further in view of Rojanasakul (cited in the Office action mailed 10 March 2003).

The claims are drawn to a computer program on media that executes a cell image analysis method comprising steps of receiving images of components of a plurality of cells of different types that have been manipulated by application of an antisense polynucleotide, producing descriptors that include information from cells of different types, and predicting properties of a compound based on its effect on cells.

Pauwels et al. in view of Paull et al. as applied to claims 49-57, 60, 61, and 63-65 above, does not show application of antisense oligonucleotides to cells.

Rojanasakul shows in the abstract and throughout that antisense oligonucleotides can be used to modulate gene expression and has potential to be used as a therapeutic for human diseases.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the program of Pauwels et al. in view of Paull et al. as applied to claims 49-57, 60, 61, and 63-65 above by use of cells treated with antisense oligonucleotides because Rojanasakul shows that antisense oligonucleotides have potential as therapeutic drugs and manipulation of cells with antisense oligonucleotides allows for study of their effects on cell lines and for comparison with the effects of other drugs.

(10) Response to Argument

The appellants point to a number of passages in the specification in support of written description of composite descriptors. The appellants point to the region of page 3, line 7 which recites:

The code determines one or more features for two or more cell components, or markers, in the presence of the substance. The code can form one or more descriptors from the features. Descriptors can be formed by combining features of two or more cell components as identified using the markers.

The region of page 3, line 7 does not describe a single composite descriptor that combines the features of two cell types.

The appellants point to the amendment of 09 August 2004 to the region of page 12, line 27 which recites:

Then, in a step 204. one or more descriptors of a state in the portions of the cells in the presence of the manipulation can be determined based upon the images collected by the imaging system. Descriptors can comprise scalar or vector values, representing quantities such as area, perimeter, dimensions, intensity, aspect ratios, and the like. Other types of descriptors include one or any combination of characteristics such as a cell count, an area, a perimeter, a length, a breadth, a fiber length, a fiber breadth, a shape factor, an elliptical form factor, an inner radius, an outer radius, a mean radius, an equivalent radius, an equivalent sphere volume, an equivalent prolate volume, an equivalent oblate volume, an equivalent sphere surface area, an average intensity, a total intensity and an optical density. In some embodiments, descriptors can include averages or standard deviation values, or frequency statistics from other descriptors collected across a population of cells. In some embodiments, descriptors can be reduced using techniques such as principal component analysis and the like. In some embodiments, the descriptors include features from different cell portions or cell types. A presently preferable embodiment uses descriptors selected from the following table. Other descriptors can also be used without departing from the scope of the invention.

The amendment of 09 August 2004 does not describe a single composite descriptor that combines features of two cell types.

The appellants point to the region of page 24, lines 17-19, but do not quote the passage accurately. The passage recites:

In a presently preferred embodiment, scalar values can comprise morphometric, frequency, multi-dimensional parameters and the like, extracted from one or more fluorescence images taken from a number of cellular markers from a population of cells. A vector of two or more such scalar values extracted from a plurality of cell lines and markers grown in the same condition together comprise a unique "fingerprint" that can be incorporated into a database.

The region of page 24, lines 17-19 does not describe a single composite descriptor that combines features of two cell types.

The appellants point to the region of page 28, lines 1-6, but do not quote the passage accurately. The passage recites:

These experiments were performed by growing multiple cell lines in the presence of multiple compounds, or substances. A fix and stain of cells using antibodies or labels to multiple cellular markers was performed. One or more images of the cells were then obtained using a digital camera. Indications were built by quantifying and/or qualifying patterns of each marker in the cell lines under study. A database was built from the indications.

The region of page 28, lines 1-6 does not describe a single composite descriptor that combines features of two cell types.

The appellants point to the region of page 18, line 28 to page 19 line 4, but do not quote the passage accurately. The passage recites:

In a particular embodiment according to the present invention, data analysis techniques for describing the fluorescence patterns of markers in multiple cell lines in the presence and absence of compounds are provided. Automated image analysis techniques can include determining one or more regions from around nuclei, individual cells, organelles, and the like, called "objects" using a thresholding function. Objects that reside on the edge of an image can be included or excluded in various embodiments. An average population information about an object can be determined and recorded into a database, which can comprise an Excel spreadsheet, for example. However,

embodiments can use any recording means without departing from the scope of the present invention. Values measured can be compared to the visual image. One or more types of numerical descriptors can be generated from the values.

The region of page 18, line 28 to page 19 line 4 does not describe a single composite descriptor that combines features of two cell types.

The appellants state that Pauwels et al. at page 109, lines 10-15 teaches away from using the method of Paull et al. However a review of the references does not support the applicant's characterization of the teachings of Pauwels et al. Pauwels et al. initially screened three cell lines, by treatment of each cell line with alternate drugs, as shown in figures 1 and 2, measuring a single parameter consisting of DNA content ("monovariate" analysis). Pauwels et al. concluded on page 109 that different classes of drugs could not be distinguished by a monovariate analysis of a single cell line. Pauwels et al. then proceeded to utilize a multivariate analysis in which each of three cell lines were treated with alternative drugs and analyzed for multiple parameters, as shows in figures 3-5. Pauwels et al. concluded that the multivariate analysis of a single cell line allows for different classes of drugs to be distinguished. Paull et al. employed a different approach to classify drugs, by use of 49 different cell lines that were treated with each alternative drug studied. Each cell line was analyzed for a single parameter of growth inhibition (see Table 1). Paull et al. used the computer program COMPARE to compare the pattern of growth inhibition of each assayed drug over multiple cell lines. Paull et al. concluded that their method allows for different classes of drugs to be distinguished, as shown in Table 2. Because Pauwels et al. (which groups drugs by detection of multiple parameters of a single cell line treated with different drugs) did not employ or mention the strategy of Paull et al. (which groups drugs by detection of a single parameter of multiple cell lines treated for each drug) it cannot be said that

Pauwels et al. teaches away from the method of Paull et al, as the applicants have stated. Because each reference shows advantages to different approaches, and the two different approaches are not conflicting and can both be used to distinguish classes of drugs, it would be obvious to combine the two methods as discussed above.

It is further noted that the argument that Pauwels et al. teaches away was made by the applicants in their response filed 30 December 2004. The argument that Pauwels et al. teaches away was rebutted in the final rejection mailed 10 March 2005. The amended appeal brief filed 20 September 2005 does not address the rebuttal to the argument that Pauwels et al. teaches away.

The appellants further state that there is no motivation to combine Rojanasakul with Pauwels et al. and Paull et al. However motivation to combine Rojanasakul is noted in the above rejection.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted

John S. Brusca John S. Brusca 21 December 2005

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